CLAIMS

What is claimed is:

1. An oligonucleotide array comprising one or more oligonucleotide tags fixed to a solid substrate, wherein each oligonucleotide tag comprises a unique known arbitrary nucleotide sequence of sufficient length to hybridize to a locus-specific tagged oligonucleotide, wherein the locus-specific tagged oligonucleotide has at its first end nucleotide sequence which hybridizes to, e.g., is complementary to, the arbitrary sequence of the oligonucleotide tag.

2. A kit comprising:

   (a) an array comprising one or more oligonucleotide tags fixed to a solid substrate, wherein each oligonucleotide tag comprises a unique known arbitrary nucleotide sequence of sufficient length to hybridize to a locus-specific tagged oligonucleotide; and

   (b) one or more locus-specific tagged oligonucleotides, wherein each locus-specific tagged oligonucleotide has at its first (5') end nucleotide sequence which hybridizes to, e.g., is complementary to, the arbitrary sequence of a corresponding oligonucleotide tag on the array, and has at it's second (3') end nucleotide sequence complementary to target polynucleotide sequence in a sample.

3. A method of genotyping a nucleic acid sample at one or more loci, comprising the steps of:

   (a) obtaining a nucleic acid sample to be tested;

   (b) combining the nucleic acid sample with one or more locus-specific tagged oligonucleotides under conditions suitable for hybridization of the nucleic acid sample to one or more locus-specific tagged

oligonucleotides, wherein each locus-specific tagged oligonucleotide comprises a nucleotide sequence capable of hybridizing to a complementary sequence in an oligonucleotide tag and a nucleotide sequence complementary to the nucleotide sequence 5' of a nucleotide to be queried in the sample, thereby creating an amplification product-locus-specific tagged oligonucleotide complex;

(c) subjecting the complex to a single base extension reaction, wherein the reaction results in the addition of a labeled ddNTP to the locus-specific tagged oligonucleotide, and wherein each type of ddNTP has a label that can be distinguished from the label of the other three types of ddNTPs;

(d) contacting the complex with an oligonucleotide array comprising one or more oligonucleotide tags fixed to a solid substrate under suitable hybridization conditions, wherein each oligonucleotide tag comprises a unique arbitrary sequence complementary and of sufficient length to hybridize to a complementarysequence in a locus-specific tagged oligonucleotide, whereby the complex hybridizes to a specific oligonucleotide tag on the array; and assaying the array to determine the labeled ddNTPs present in the complex hybridized to one or more oligonucleotide tags,

thereby determining the genotype of the queried nucleotide in the sample.

4. A method to aid in determining a ratio of alleles at a polymorphic locus in a sample, comprising the steps of:

(a) using a pair of primers to amplify a region of a nucleic acid in a sample, wherein the region comprises a polymorphic locus, whereby an amplified DNA product is formed;

(b) labeling an extension primer by a single base extension reaction to form a labeled extension primer, wherein the amplified DNA product is used as a template, wherein the extension primer comprises a 3' portion and a

5' portion, wherein the 3' portion is complementary to the amplified DNA product and terminates one nucleotide 5' to the polymorphic locus, wherein the 5' portion is not complementary to the amplified DNA product, whereby a labeled dideoxynucleotide which is complementary to the polymorphic locus is coupled to the 3' end of the extension primer, wherein each type of dideoxynucleotide present in the reaction bears a distinct label; and

(c) hybridizing the 5' portion of the extension primer to one or more probes complementary to the 5' portion which are immobilized to known locations on a solid support.

5. The method of claim 4 wherein two complementary strands of the amplified DNA product are present in the single base extension reaction.

6. The method of claim 4 wherein two complementary strands of the amplifed DNA product are used as templates in the step of labeling.

7. The method of claim 4 wherein the label is a fluorescent label.

8. The method of claim 4 wherein the label is a radiolabel.

9. The method of claim 4 wherein the label is an enzyme label.

10. The method of claim 4 wherein the label is an antigenic label.

11. The method of claim 4 wherein the label is an affinity binding partner.

12. The method of claim 4 further comprising the step of:

(d) optically detecting a fluorescent label on the solid support.

13. The method of claim 4 wherein the step of labeling employs at least two distinct dideoxynucleotides bearing distinct labels.

14. The method of claim 4 wherein the step of labeling employs four distinct dideoxynucleotides bearing distinct labels.

15. The method of claim 4 further comprising the steps of:

(d) comparing quantities of a first and a second label at a location on the solid support; and

(e) determining the ratio of nucleotides present at the polymorphic locus in the sample.

16. The method of claim 15 wherein the ratio of nucleotides present at two or more polymorphic loci is determined simultaneously.

17. The method of claim 4 wherein the sample comprises DNA from two or more individuals.

18. The method of claim 17 wherein the ratio of nucleotides present at two or more polymorphic loci is determined simultaneously.

19. The method of claim 4 wherein the solid support is selected from the group consisting of beads, microtiter plates, and oligonucleotide arrays.

20. A set of primers for use in determining a ratio of nucleotides present at a polymorphic locus, comprising:

(a) a pair of primers which when in the presence of a DNA polymerase amplify a region of double stranded DNA, wherein the region comprises a polymorphic locus; and

DO NOT ENTER

(b) an extension primer which comprises a 3' portion which is complementary to a portion of the region of double stranded DNA and a 5' portion which is not complementary to the region of double stranded DNA, wherein the extension primer terminates one nucleotide 5' to the polymorphic locus.

21. A kit comprising in a single container two or more of the sets of primers of claim 20.

22. A kit comprising in a single container:

(a) a set of primers of claim 20; and

(b) a solid support comprising a probe which is attached to a solid support, wherein the probe is complementary to the 5' portion of the extension primer.

23. The kit of claim 22 wherein the solid support is an oligonucleotide array.

24. The kit of claim 22 wherein the solid support is a bead.

25. The kit of claim 22 wherein the solid support is a microtiter plate.

26. A method to aid in determining a ratio of alleles at a polymorphic locus in a sample, comprising the steps of:

(a) labeling an extension primer by a single base extension reaction to form a labeled extension primer, using a DNA molecule as a template, wherein the extension primer comprises a 3' portion and a 5' portion, wherein the 3' portion is complementary to the DNA molecule and terminates one nucleotide 5' to a polymorphic locus, wherein the 5' portion is not complementary to the DNA molecule, whereby a labeled

dideoxynucleotide which is complementary to the polymorphic locus is coupled to the 3' end of the extension primer, wherein each type of dideoxynucleotide present in the reaction bears a distinct label; and

(b) hybridizing the 5' portion of the extension primer to one or more probes complementary to the 5' portion which are immobilized to known locations on a solid support.

27. The method of claim 26 wherein two complementary strands of the DNA molecule are present in the single base extension reaction.

28. The method of claim 27 wherein each complementary strand of the DNA molecule is used as a template to label an extension primer.

29. The method of claim 26 wherein the label is a fluorescent label.

30. The method of claim 26 wherein the label is a radiolabel.

31. The method of claim 26 wherein the label is an enzyme label.

32. The method of claim 26 wherein the label is an antigenic label.

33. The method of claim 26 wherein the label is an affinity binding partner.

34. The method of claim 26 further comprising the step of:

(c) optically detecting a fluorescent label on the solid support.

35. The method of claim 26 further comprising the steps of:

(c) comparing quantities of a first and a second label at a location on the solid support; and

DOCKET ALARM

(d) determining the ratio of nucleotides present at the polymorphic locus in the sample.

36. The method of claim 35 wherein the ratio of nucleotides present at two or more polymorphic loci is determined simultaneously.

37. The method of claim 26 wherein the sample comprises DNA from two or more individuals.

38. The method of claim 34 wherein the ratio of nucleotides present at two or more polymorphic loci is determined simultaneously.

39. The method of claim 26 wherein the step of labeling employs at least two distinct dideoxynucleotides bearing distinct labels.

40. The method of claim 26 wherein the step of labeling employs four distinct dideoxynucleotides bearing distinct labels.